UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/882,843	06/15/2001	Xue-Feng Pei	SYM 114	8772

7590 09/25/2002

Holland & Knight LLP
Suite 2000
1201 West Peachtree Street, N.E.
Atlanta, GA 30309

EXAMINER	
COLEMAN, BRENDA LIBBY	
ART UNIT	PAPER NUMBER
1624	7

DATE MAILED: 09/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/882,843	PEI et al.
Examiner	**Art Unit**
Brenda Coleman	1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-30 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-30 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-30 are pending in the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 3, 4, 6-15, 18, 19, 21-27, 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for ischaemia, does not reasonably provide enablement for "neurological diseases". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The scope of "neurological, neuropsychological, neuropsychiatric, neurodegenerative, neuropsychopharmacological and functional disorders" cannot be deemed enabled. The term "neurological, neuropsychological, neuropsychiatric, neurodegenerative, neuropsychopharmacological and functional disorders" covers a broad array of different disorders that have different modes of action and different origins. The term covers such diverse disorders as Alzheimer's Disease; Parkinson's Disease; ALS and variants such as forms of ALS-PDC; Gerstmann-Straussler-Scheinker Disease (GSS); Pick's Disease; Diffuse Lewy Body Disease; Hallervordon-Spatz disease; progressive familiar myoclonic epilepsy; Corticodentatonigral degeneration; progressive supranuclear palsy (Steele-Richardson-Olszewski); Huntington's disease; more than a dozen dementias collectively called

"frontotemporal dementia and Parkinsonism linked to chromosome 17" (FTDP-17); Tourette's syndrome; Shy-Drager syndrome; Friedrich's ataxia and other spinocerebellar degenerations; Olivopontocerebellar atrophy (OPCA); spasmotic torticollis; Striatonigral degeneration; various types of torsion dystonia; certain spinal muscular atrophies, such as Werdnig-Hoffmann and Wohlfart-Kugelberg-Welander; Hereditary spastic paraplegia, Primary lateral sclerosis; peroneal muscular atrophy (Charcot-Marie-Tooth); Creutzfeldt-Jakob Disease (CJD); Hypertrophic interstitial polyneuropathy (Dejerine-Sottas); retinitis pigmentosa; Leber's Disease; and Hypertrophic interstitial polyneuropathy. These exhibit a very broad range of effects and origins. For example, some give progressive dementia without other prominent neurological signs, such as Alzheimer's Disease, whereas other dementias have such signs, such as Diffuse Lewy Body Disease. Some give muscular wasting without sensory changes, e.g. ALS, and some do have the sensory changes such as Werdnig-Hoffmann. Some are abnormalities of posture, movement or speech, such as Striatonigral degeneration, and other are progressive ataxias, such as OPCA. Some are linked to tau mutations, such as Alzheimer's Disease and FTDP-17, and other such as Parkinson's clearly do not. Some affect only vision such as retinitis pigmentosa. Even within those that fall into the same category of effects, there are often striking differences. For example, Alzheimer's Disease and Pick's disease both give progressive dementia without other prominent neurological signs. But the characteristic Alzheimer's neurofibrillary tangles are not seen in Pick's Disease, which has straight fibrils, as opposed to the paired helical filaments of Alzheimer's Disease. Pick's Disease gives lobal atrophy, not seen in Alzheimer's Disease. There are differences

in origins, even with what little is known. Thus, among progressive dementias, CJD is definitely caused by an infectious agent; so far as can be determined, this is not so for Huntington's disease. Even among the hereditary disorders, the origins are different. Thus, FTDP-17 comes from chromosome 17, Huntington's Disease from 4, and the neurodegenerative disorder that people with Down's syndrome develop later in life is presumably connected in some way to 21.

The great majority of these have no treatment at all, and of those that do, none or virtually none have been treated with such inhibitors as are disclosed here. The great diversity of diseases falling within the "neurological, neuropsychological, neuropsychiatric, neurodegenerative, neuropsychopharmacological and functional disorders" category means that it is contrary to medical understanding that any agent (let alone a genus of trillions of compounds) could be generally effective against such diseases. The intractability of these disorders is clear evidence that the skill level in this art is low relative to the difficulty of the task. Further, what little success there has been does not point in this direction. Thus, what very few treatments that the massive research effort on Alzheimer's Disease has produced are means of providing Acetylcholinesterase inhibition, unrelated to the mechanism of action in this case.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a) A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. Claims are pending in the application.. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. Claims are pending in the application.. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. Claims are pending in the application.. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. Claims are pending in the application.. 1949). In the present instance, claims 1-4, 8-12, 15-19, 23-27 and 30 recite the broad recitation halogen in the definition of R^1, R^2, R^3 and R^4, and the claim also recites (F, Cl, Br) which is the narrower statement of the range/limitation.

b) Claims 1-4, 8-12, 15-19, 23-27 and 30 are vague and indefinite in that it is not known what is meant by the proviso, where one of R^1, R^2, R^3 and R^4 **must be** C1-C3-alkoxy or C1-C3-alkylthio. At no time can R^1, R^2, R^3 and R^4 be C1-C3-alkylthio.

c) A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. Claims are pending in the application.. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. Claims are pending in the application.. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. Claims are pending in the application.. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. Claims are pending in the application.. 1949). In the present instance, claims 1-4, 8-12, 15-19, 23-27 and 30 recite the broad recitation halogen in the definition of the substituents on the phenyl ring within the definition of R^5, R^6, R^7 and R^8 with

respect to Formula I and R^5, R^6 and R^7 with respect to Formula II and the claim also recites (F, Cl, Br) which is the narrower statement of the range/limitation.

d) A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. Claims are pending in the application.. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. Claims are pending in the application.. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. Claims are pending in the application.. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. Claims are pending in the application.. 1949). In the present instance, claims 1-4, 8-12, 15-19, 23-27 and 30 recite the broad recitation halogen in the definition of R^{12} with respect to Formula I and R^{18} and R^{19} with respect to Formula II and the claim also recites (F, Cl, Br) which is the narrower statement of the range/limitation.

e) Claim 2 recites the limitation "$R^{13}S$-" in the definition of R^1, R^2, R^3 and R^4. There is insufficient antecedent basis for this limitation in the claim.

f) Claim 3 is vague and indefinite in that it is not known what is meant by the compound of claim 2 in addition to a pharmaceutically acceptable carrier. It is not known if this is a compound claim or a pharmaceutical composition of the compounds of Formula I and a pharmaceutically acceptable carrier.

g) Claim 4 is a substantial duplicate of claim 3, as the only difference is a statement of intended use which is not given material weight. Note In re Tuominen 213 USPQ 89.

h) Claims 3, 4, 6-15, 18, 19, 21-27, 29 and 30 are vague and indefinite in that the claim provides for the use of claimed compounds, but the claim does not set forth any steps involved in determining which are the diseases capable of being mediated by inhibiting the activity of the α-amino-3-hydroxy-5-methyl-4-isooxazolepropionic acid (AMPA) subtype of the ionotropic excitatory amino acid (EAA) receptor. It is unclear which diseases are mediated by inhibiting the activity of the α-amino-3-hydroxy-5-methyl-4-isooxazolepropionic acid (AMPA) subtype of the ionotropic excitatory amino acid (EAA) receptor? Determining whether a given disease responds or does not respond to such an inhibitor will involve undue experimentation. Suppose that a given drug, which has inhibitor properties *in vitro*, when administered to a patient with a certain disease, does not

produce a favorable response. One can not conclude that specific disease does not fall within this claim. Keep in mind that:

A. It may be that the next patient will respond. No pharmaceutical has 100% efficacy. What success rate is required to conclude our drug is a treatment? Thus, how many patients need to be treated? If "successful treatment" is what is intended, what criterion is to be used? If one person in 10 responds to a given drug, does that mean that the disease is treatable? One in 100? 1,000? 10,000? Will the standard vary depending on the current therapy for the disease?

B. It may be that the wrong dosage or dosage regimen was employed. Drugs with similar chemical structures can have markedly different pharmacokinetics and metabolic fates. It is quite common for pharmaceuticals to work and or be safe at one dosage, but not at another that is significantly higher or lower. Furthermore, the dosage regimen may be vital --- should the drug be given e.g. once a day, or four times in divided dosages? The optimum route of administration can not be predicted in advance. Should our drug be given as a bolus *iv* or in a time release *po* formulation. Thus, how many dosages and dosage regimens must be tried before one is certain that our drug is not a treatment for this specific disease?

C. It may be that our specific drug, while active *in vitro*, simply is not potent enough or produces such low concentrations in the blood that it is not an

effective treatment of the specific disease. Perhaps a structurally related drug is potent enough or produces high enough blood concentrations to treat the disease in question, so that the first drug really does fall within the claim. Thus, how many different structurally related inhibitors must be tried before one concludes that a specific compound does not fall within the claim?

D. Conversely, if the disease responds to our second drug but not to the first, both of whom are inhibitors *in vitro*, can one really conclude that the disease falls within the claim? It may be that the first compound result is giving the accurate answer, and that the success of second compound arises from some other unknown property which the second drug is capable. It is common for a drug, particularly in neurologicals, to work by many mechanisms. The history of psychopharmacology is filled with drugs, which were claimed to be a pure receptor XYX agonist or antagonist, but upon further experimentation shown to effect a variety of biological targets. In fact, the development of a drug for a specific disease and the determination of its biological site of action usually precede linking that site of action with the disease. Thus, when mixed results are obtained, how many more drugs need be tested?

E. Suppose that our drug is an effective treatment of the disease of interest, but only when combined with some totally different drug. There are for example, agents in antiviral and anticancer chemotherapy which are not themselves

effective, but are effective treatments when the agents are combined with something else.

Consequently, determining the true scope of the claim will involve extensive and potentially inconclusive research. Without it, one skilled in the art cannot determine the actual scope of the claim. Hence, the claim is indefinite.

i) Claim 5 is vague and indefinite in that it is not known what is meant by second occurrence of the species 1-(4-Aminophenyl)-3,5-dihydro-4-methyl-3-acetyl-8-methoxy-5*H*-2,3-benzodiazepine. See lines 2-3 and lines 14-15 on page 40.

j) Claim 5 recites the limitation "8-amino" in several species. There is insufficient antecedent basis for this limitation in the claim. See lines 8-14 on page 40 and lines 3-11 on page 41.

k) Claim 5 recites the limitation "7-amino" in several species. There is insufficient antecedent basis for this limitation in the claim. See lines 20-27 on page 40 and lines 17-23 on page 41.

l) Claim 5 recites the limitation "7-methylthio" in several species. There is insufficient antecedent basis for this limitation in the claim. See line 27 on page 40 through line 11 on page 41.

m) Claim 5 recites the limitation "8-methylthio" in several species. There is insufficient antecedent basis for this limitation in the claim. See lines 11-24 on page 41.

n) Claim 6 is vague and indefinite in that it is not known what is meant by the compound of claim 5 in addition to a pharmaceutically acceptable carrier. It is not known if this is a compound claim or a pharmaceutical composition of the compounds of formula I and a pharmaceutically acceptable carrier.

o) Claim 7 is a substantial duplicate of claim 6, as the only difference is a statement of intended use which is not given material weight. Note In re Tuominen 213 USPQ 89.

p) Claim 8 is vague and indefinite in that it is not known what is meant by the compound of claim 1 in addition to a pharmaceutically acceptable carrier. It is not known if this is a compound claim or a pharmaceutical composition of the compounds of Formula I and a pharmaceutically acceptable carrier.

q) Claim 9 is a substantial duplicate of claim 8, as the only difference is a statement of intended use which is not given material weight. Note In re Tuominen 213 USPQ 89.

r) Claim 11 recites the limitation "$R^{13}S$-" in the definition of R^1, R^2, R^3 and R^4. There is insufficient antecedent basis for this limitation in the claim.

s) Claim 13 is vague and indefinite in that it is not known what is meant by second occurrence of the species 1-(4-Aminophenyl)-3,5-dihydro-4-methyl-3-acetyl-8-methoxy-5*H*-2,3-benzodiazepine. See lines 4-5 of claim 13 and lines 16-17 of claim 13.

t) Claim 13 recites the limitation "8-amino" in several species. There is insufficient antecedent basis for this limitation in the claim. See lines 10-16 and lines 35-43 of claim 13.

u) Claim 13 recites the limitation "7-amino" in several species. There is insufficient antecedent basis for this limitation in the claim. See lines 22-29 and 49-56 of claim 13.

v) Claim 13 recites the limitation "7-methylthio" in several species. There is insufficient antecedent basis for this limitation in the claim. See lines 29-43 of claim 13.

w) Claim 13 recites the limitation "8-methylthio" in several species. There is insufficient antecedent basis for this limitation in the claim. See lines 43-56 of claim 13.

x) Claim 16 is vague and indefinite in that it is not known what is meant by the definition of R^{17} on page 50, since there is no variable R^{17} within Formula II.

y) Claim 17 recites the limitation "$R^{13}S$-" in the definition of R^1, R^2, R^3 and R^4. There is insufficient antecedent basis for this limitation in the claim.

z) Claim 18 is vague and indefinite in that it is not known what is meant by the compound of claim 17 in addition to a pharmaceutically acceptable carrier. It is not known if this is a compound claim or a pharmaceutical composition of the compounds of Formula II and a pharmaceutically acceptable carrier.

aa) Claim 19 is a substantial duplicate of claim 18, as the only difference is a statement of intended use which is not given material weight. Note In re Tuominen 213 USPQ 89.

ab) Claim 20 recites the limitation "8-amino" in several species. There is insufficient antecedent basis for this limitation in the claim. See lines 3-4 and lines 7-8 of claim 20.

ac) Claim 20 recites the limitation "7-amino" in several species. There is insufficient antecedent basis for this limitation in the claim. See lines 5-6 and 9-10 of claim 20.

ad) Claim 20 recites the limitation "7-methylthio" in several species. There is insufficient antecedent basis for this limitation in the claim. See lines 6-8 of claim 20.

ae) Claim 20 recites the limitation "8-methylthio" in several species. There is insufficient antecedent basis for this limitation in the claim. See lines 8-10 of claim 20.

af) Claim 21 is vague and indefinite in that it is not known what is meant by the compound of claim 20 in addition to a pharmaceutically acceptable carrier. It is not known if this is a compound claim or a pharmaceutical composition of the compounds of Formula II and a pharmaceutically acceptable carrier.

ag) Claim 22 is a substantial duplicate of claim 21, as the only difference is a statement of intended use which is not given material weight. Note In re Tuominen 213 USPQ 89.

ah) Claim 23 is vague and indefinite in that it is not known what is meant by the compound of claim 16 in addition to a pharmaceutically acceptable carrier. It is not known if this is a compound claim or a pharmaceutical composition of the compounds of Formula II and a pharmaceutically acceptable carrier.

ai) Claim 24 is a substantial duplicate of claim 23, as the only difference is a statement of intended use which is not given material weight. Note In re Tuominen 213 USPQ 89.

aj) Claim 25 is vague and indefinite in that it is not known what is meant by the definition of R^{17} on page 50, since there is no variable R^{17} within Formula II.

ak) Claim 26 recites the limitation "$R^{13}S$-" in the definition of R^1, R^2, R^3 and R^4. There is insufficient antecedent basis for this limitation in the claim.

al) Claim 28 recites the limitation "8-amino" in several species. There is insufficient antecedent basis for this limitation in the claim. See lines 3-4 and lines 7-8 of claim 28.

am) Claim 28 recites the limitation "7-amino" in several species. There is insufficient antecedent basis for this limitation in the claim. See lines 5-6 and 9-10 of claim 28.

an) Claim 28 recites the limitation "7-methylthio" in several species. There is insufficient antecedent basis for this limitation in the claim. See lines 6-8 of claim 28.

ao) Claim 28 recites the limitation "8-methylthio" in several species. There is insufficient antecedent basis for this limitation in the claim. See lines 8-10 of claim 28.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 16-19, 23 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Rona et al., Journal of Chromatography B: Biomedical Applications. Rona teaches the compounds and compositions of the instant invention where R^1 is hydrogen, R^2 is methoxy, R^3 is methoxy, R^4 is hydrogen, R^5 is hydrogen, R^6 is hydrogen, R^7 is methyl, R^{18} is hydrogen, R^{19} is hydrogen, R^{20} is $NHC(=O)CH_3$ or NH_2, and R^{21} is hydrogen. See Figure 1.

4. Claims 16-19, 23-27 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Lang et al., U.S. Patent No. 4,614,740. Lang teaches the compounds, compositions and method of use of the instant invention where R^1 is hydrogen, R^2 is methoxy or ethoxy, R^3 is methoxy or

ethoxy, R^4 is hydrogen, R^5 is hydrogen, methyl or ethyl, R^6 is hydrogen, R^7 is methyl, R^{18} is hydrogen or chloro, R^{19} is hydrogen, chloro or methyl, R^{20} is hydrogen or NH_2, and R^{21} is hydrogen or NH_2. See examples 1, 2, 4, 10-13, 16-18, etc.

5. Claims 1-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Ling et al., WO 97/28135. Ling teaches the compounds, compositions and method of use of the instant invention where R^1 is hydrogen, R^2 is methoxy, R^3 is hydrogen, bromo or chloro, R^4 is hydrogen, R^5 is hydrogen, R^6 is hydrogen, R^7 is methyl, R^8 is hydrogen, R^9 is $C(=O)CH_3$, $C(=O)NHCH_3$, $C(=O)CH_2CH_3$, C(=O)cyclopropyl, $C(=O)OCH_3$, R^{10} is NH_2, R^{11} is hydrogen and R^{12} is hydrogen for Formula I and R^{18} is hydrogen, R^{19} is hydrogen, R^{20} is NH_2, and R^{21} is hydrogen for Formula II. See examples 3-9 and claim 2.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 16-19, 23-27 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lang et al., U.S. Patent No. 4,614,740. The generic structure of Lang encompasses the instantly claimed compounds (see Formula I, column 1) and for the same uses as claimed herein. Examples 1, 2, 4, 10-13, 16-18, etc. which anticipates some of the claims as discussed in the

above 102 rejection differ only in the nature of the R, R_1, R_2, R_3 and R_4 substituents. Column 1, lines 29-33 defines the substituent R and R_1 each represent hydrogen, chlorine, C_{1-4} alkyl or C_{1-4} alkoxy, R_2 stands for hydrogen or C_{1-4} alkyl, and R_3 and R_4 each denote C_{1-4} alkyl, or combined they denote methylene. Compounds of the instant invention are generically embraced by Lang in view of the interchange ability of R, R_1, R_2, R_3 and R_4 substituents of the bicyclic ring system. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select for example R_3 and R_4 are propyl or butyl as well as other possibilities from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

7. Claims 1-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ling et al., WO 97/28135. The generic structure of Ling encompasses the instantly claimed compounds (see Formula I, page 1) and for the same uses as claimed herein. Examples 3-9 and the species of claim 2 which anticipates some of the claims as discussed in the above 102 rejection differ only in the nature of the X, Y, R^1, R^2, R^4, R^5 and R^6 substituents. Page 1 defines the substituent X designates hydrogen or halogen, Y designates $-NR^3-$ or -N= where R^3 designates hydrogen, $-COR^{10}$, C_{1-6} alkyl or C_{3-7} cycloalkyl, R^1 and R^2 designates hydrogen, C_{1-6} alkyl, nitro, halogen, $-NR^8R^9$, $-O-C_{1-4}$ alkyl, CF_3, OH or C_{1-6} alkanoyloxy, R^4 designates an optionally substituted C_{1-6} alkyl, R^5 designates hydrogen or with R^6 is =O and R^6 designates C_{1-4} alkyl. Compounds of the instant invention are generically embraced by Ling in view of the interchange ability of X, Y, R^1,

R^2, R^4, R^5 and R^6 substituents of the bicyclic ring system. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select for example R^2 is trifluoromethyl as well as other possibilities from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is (703) 305-1880. The examiner can normally be reached on Mondays and Tuesdays from 9:00 AM to 3:00 PM and from 5:30 PM to 7:30 PM and on Wednesday thru Friday from 9:00 AM to 6:00 PM.

The fax phone number for this Group is (703) 308-4734 for "unofficial" purposes and the actual number for **OFFICIAL** business is **308-4556**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brenda Coleman

Brenda Coleman
Primary Examiner AU 1624
September 23, 2002